Remarks

Claims 1-7 and 9-19 are pending currently in this application; with claim 1 and2 being amended.

Claim 8 has been canceled to obviate the objection thereto under 37 CFR § 1.75(c).

Applicants respectfully reserve the right to file a divisional patent application to subject matter that has deleted by amendment or cancellation from that originally pending.

Claim 1 has been amended to replacce the term "exposing" with the phrase "bringing the motoneurons into contact with" as suggested by the examiner. Support for the amendment is found throughout the specification, e.g., see the examples at pages 6-7 of the specification.

Claim 2 has been amended to change it from a method of preventing to a method of treating. Support for the amendment is found throughout the specification, for example at page 1, lines 3-4.

The amendments of claims 1 and 2 do not add any new matter.

I. Objection of Claim 8 under 37 CFR § 1.75(c)

The Examiner objected to claim 8 for the following:

> ... as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 8 recites how the low molecular weight heparin is obtained. The recitation is not further limiting. It does not matter how the heparin is obtained.

Current Office Action, at page 2, 1st paragraph.

Applicants respectfully traverse the objection. Claim 8 has been canceled to obviate the objection. Thus, applicants respectfully request the reconsideration and withdrawal of the objection.

II. Rejection of Claims 2-19 under 35 USC § 112, First Paragraph

The Examiner rejected Claims 2-19 for the following:

... because the specification, while being enabling for treating motoneuron diseases, does not reasonably provide enablement for prevention of motoneuron diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of one of ordinary skill
(D) The level of predictability in the art
(E) The amount of direction provided by the inventor
(F) The existence of working examples
(G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claims 2-19 are drawn to a method for preventing a motoneuron disease in a patient comprising administering an effective amount of low molecular weight heparin, with specific molecular weights. The scope of the claim is seen to include the administration of the said compound to a healthy patient, and subsequent exposure to conditions that would cause the motoneuron disease, wherein the said compound prevents the said exposure from manifesting itself in said patient so exposed.

The state of the prior art

The examiner notes that the art cited by the applicants mentions methods for preparing heparins and use of the same in treating thrombosis. Snow et al (WO 91/06303) drawn to glycosaminoglycans and proteoglycans, disclose the use of these compounds for the regeneration/treatment of neurons damaged by disorders like amyotrophic lateral sclerosis. However, there is no disclosure of potential motoneuron disease preventive activity of the compound seen in the prior art. The prior art appears to be silent with regard to preventive procedures recognized by skilled artisans in the field.

The level of one of ordinary skill

The skilled artisan in this field is that of an MD for chemotherapeutic administration and/or a Ph.D. skilled in the development of chemotherapeutics.

The level of predictability in the art

The examiner acknowledges the probability and predictability that administration of the said compounds would have a reasonable expectation of success for preventing the said disease. There is not seen sufficient data to substantiate the assertion that the said disease may be prevented by the use of the compound as instantly claimed.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the use of the active agents to prevent motoneuron disease. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for an advance in treating motoneuron disease which induces prevention of the said disease.

The existence of working examples

The working examples set forth in the instant specification are drawn to data involving cells in vitro. The skilled artisan in this field would not extrapolate the preventive efficacy of the compound claimed or the use of the same in preventive methods from just this example provided. The disclosure does not show the prevention of motoneuron disease.

However, it is seen to show the effect of the active agents.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the prevention of motoneuron disease with the compound set forth in the claims. A skilled artisan would not extrapolate the preventive efficacy from the results disclosed in the examples, set forth in the instant specifications.

Current Office Action, at page 2, 1st paragraph.

Applicants respectfully traverse the rejection. Claim 2-7 and 9-19 have been amended to obviate the rejection. More particularly, Applicants have amended claim 2, and thus claims dependent there from, by there being directed now to a method of treating rather than a method of preventing. The method of treating is noted by the Examiner in the 1st paragraph of this rejection to be supported versus the method of preventing, and thus Applicants have amended the claims to that which is acknowledged to be supported. In view of the noted amendment, Applicants respectfully request the reconsideration and withdrawal of the rejection.

III. Rejection of Claims 2-19 under 35 USC § 112, First Paragraph

The Examiner rejected Claims 2-19 for the following:

Claim 1 recites the term "exposing". It is not clear what this means. If it means bringing the motoneurons in contact with the heparin then the claim should be reworded to indicate this. Clarification is needed.

Claims 18 and 20 recite alphanumeric notations for the heparins. It is not clear what these notations mean. Perusal of the specification failed to clarify this either. The notations should be replaced with a chemical name or structure.

Claims, which depend from rejected base claims that are unclear or indefinite, are also rendered unclear or indefinite.

Office Action at page 5

Applicants respectfully traverse the rejection.

Though Applicants submit that the term "exposing" in claim 1 was clear, Applicants have amended claim 1 to recite the language suggested by the Examiner. Such should render moot the rejection. In view of the noted amendment, Applicants respectfully request the reconsideration and withdrawal of the rejection.

The Examiner has taken issue with the recitation of alphanumeric notations regarding heparins in claims 18 and 19.[1] Applicants submit that there is no basis for having to replace the noted designations with chemical names or structures. Applicants have provided herewith a number of references[2] that cleary evidence that those skilled in the art clearly know what those alphanumeric notations mean. Furthermore, the art is replete with examples where the alphanumeric notations are used as the primary format for describing the compounds that they relate to. Thus, more should not be needed unless the Examiner can demonstrate that those skilled in the art do not know what those alphanumeric notations refer to. In view of the noted amendment, Applicants respectfully request the reconsideration and withdrawal of the rejection.

Applicants submit also that the aforesaid remarks and amendment renders moot any rejections to claims that depend from claim 1. Thus, Applicants respectfully request the reconsideration and withdrawal of the rejection with regard to such claims due to such dependence.

IV. Rejection of Claims 1 and 3-19 Under 35 USC § 103(a) Over Snow et al.

The Examiner rejected Claims 1 and3-19 under 35 USC § 103(a) for allegedly

> Snow et al teach pharmaceutical compositions comprising effective amounts of heparin (HN)(page 11, lines 5-9) and also disclose that the compositions of their invention can be used where nerve regeneration is desired for example patients with nerve damage. The compositions can be administered to patients in whom nerve cells have been damaged by disorders like amyotrophic lateral sclerosis (page32, line 29 through page 33, line 10). However, Snow et al do not specifically disclose the use of any individual low molecular weight heparin like enoxaparin.
>
> It would have been obvious to one of ordinary skill in the art at the time the invention was made to use low molecular weight heparins to promote growth of motoneurons. Low molecular weight heparins comprise disaccharides that mimic heparin and are used as mimetics for treatment of thrombosis (Merck Index, 1996, 12th, edition, #3626 and #6434). A skilled artisan would be motivated to use a art tested low molecular weight mimetic of heparin in a method for promoting nerve growth and survival as instantly claimed.

Office Action at page 6-7, emphasis added.

Applicants respectfully traverse this rejection.

There is absolutely no disclose in cited application PCT/US90/06189 of low molecular weight heparins or how to prepare them, or suggestion that low molecular weight heparins having anti-thrombotic activity like heparin would be useful. In fact, the PCT/US90/06189 application at page 10, lines 28-30,

[1] In the Office Action the Examiner notes claims 18 and 20. This must be in error as no claim 20 exists, and claim 19 pertains to an alphanumeric compound designation like in claim 18. Thus, the rejection directed to claim 20 will be responded to as if it were to claim 19.

[2] See, Treatment of Proximal Deep Vein Thrombosis with a Novel Synthetic Compound (SR90107A/ORG31540) with pure anti-factor Xa activity: A phase II evaluation. The Rembrandt Investigators.– Circulation. 2000 Nov. 28;102(22):2726-31; Graudins, et al., Low Molecular Weight Heparins Heparinoids & Hirudins, The NSW Therapeutic Assessment Group Inc., (1999), 1-34, 8; Barradas, et al., Comparison of platelet pro-aggregatory effect of convention unfractionated heparins and a low molecular weight heparin fraction (CY 222), Br.J Haematol. 1987 Dec;67(4):451-457; and US Patent Application 6,579,858 – Use of Low-Molecular-Weight Heparins For the Prevention and Treatment of Cerebral Edemas at Col. 2, lines 17-22.

discloses that the promotion of neurite outgrowth would occur by removing the inhibitory influence of molecules comprising HN (heparin). Thus, that disclosure teaches the use of compounds that are inhibitory of heparin.[3] The aforesaid thus teaches against the use of compounds that are mimetics (mimics) of heparin.

In view of the aforesaid, Applicants request the reconsideration and withdrawal of the rejection.

In light of the above amendments and remarks, it is respectfully submitted that the present application is in condition for allowance. Early notice to this effect is, thus, respectfully requested.

Respectfully submitted,

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[3] For example, page 10, line 16-35 of the PCT/US90/06189 application only states "Such inhibitors and antagonists include but are not limited to...disaccharide antagonists of receptors specific for...HS [(heparin sulfate)], HN [(heparin sulfate)]....".